(350)

PLATELET-ENDOTHELIUM INTERACTIONS IN HUMANS: CHANGES IN PLATELET CYCLIC GUANOSINE MONOPHOSPHATE CONTENT IN PATIENTS WITH ENDOTHELIAL DYSFUNCTION

N P Andrews, N Dakak, W H Schenke, A A Quyyumi,
National Heart Lung and Blood Institute, Bethesda, MD, USA

Vascular endothelial dysfunction occurs in patients with atherosclerosis and those exposed to risk factors for atherosclerosis. These patients are also at risk for thrombotic vascular events. To investigate whether platelet-endothelium interactions vary between patients with and those without endothelial dysfunction, we studied the effect on platelet cyclic GMP content (PcGMPc) of acetylcholine (ACH) (that causes release of nitric oxide (NO) from endothelium) and compared it to the effect of sodium nitroprusside (SNP), a direct donor of NO. The platelet and vascular effects of intra-arterial ACH and SNP were studied in the femoral circulation of 19 patients, 10 with coronary atherosclerosis and 9 with angiographically normal coronary and femoral arteries. Intra-femoral arterial infusion of ACH (55 μg/min for 2 and 10 min), and SNP (40 μg/min for 2 min in 8 patients) were given and blood flow velocity was measured with intravascular doppler (Flowire, Cardiometrics Inc.). PcGMPc was measured by radioimmunoassay after withdrawing blood samples from the femoral vein. The vasodilator response to ACH was heterogenous, mean increase in flow velocity 69±57% (mean± SD), range -8% to 225%, $p<.0001$ after 2 min. Patients with atherosclerosis or multiple risk factors had depressed flow responses $p<0.05$. PcGMPc change was also heterogenous with ACH (mean change 11±35%, p=NS; range -37% to 88% increase). There was a highly significant correlation between the increase in flow velocity with ACH and the change in PcGMPc ($r=0.57$, $p<0.001$); thus, patients with depressed vasodilation did not increase PcGMPc, whereas those with good vasodilator response to ACH increased PcGMPc. In contrast, the vasodilator response to SNP (mean 113±59% increase in flow velocity) was similar in all patients and the PcGMPc increase (mean 151±141%, $p<0.02$) did not correlate with the PcGMPc responses to ACH. Thus, patients with endothelial dysfunction not only have depressed vascular smooth muscle responses to endothelial-dependent dilators due to reduced abluminal release of NO, but also have depressed luminal release of NO, as reflected by reduced PcGMP content. This may explain the susceptibility of patients with endothelial dysfunction to thrombotic vascular events.

CORRECTIONS

Posters 62 and 313 were withdrawn.